Is there a Difference in Orbital Volume Between Affected and Unaffected sides In Patients with Unilateral Craniofacial Microsomia

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Abstract

BACKGROUND: Craniofacial microsomia (CFM) is characterized by malformations of the structures derived from the first and second pharyngeal arches. The orbit is variably affected. The purpose of this study was to determine if there is a difference in orbital volume between affected and unaffected sides in patients with unilateral CFM. The specific aims were to 1) measure orbital volume 2) compare affected and unaffected sides 3) evaluate the correlation between clinical evaluation of orbital size and volumetric measurement and 4) determine whether there is a correlation between orbital volume and severity of mandibular deformity.

METHODS: Retrospective case series ~~radiographic~~ of patients with unilateral CFM from Boston Children's Hospital who had a computed tomographic scan (CT). Manual segmentation of the orbit using Mimics software was performed on CT images of both orbits. The predictor variable was laterality (affected versus unaffected side) and the primary outcome variable was orbital volume. Wilcoxon signed rank test was used to compare these measurements and determine if the affected side differed from the unaffected. Correlation between orbital volume and Pruzansky-Kaban type mandibular deformity, as documented in the medical record, was determined using the Spearman's rank correlation coefficient.

RESULTS: Thirty-nine patients were included. Orbital volume was 10% smaller on the affected side (p= 0.001) in 80% of subjects. There was no correlation between orbital size and severity of mandibular involvement.

CONCLUSION: The results of this study demonstrate a significant difference in orbital volume between affected and unaffected sides in patients with unilateral CFM. These differences were small and may not be clinically relevant. Orbital volume does not correlate with severity of the mandibular deformity.

Introduction

Craniofacial microsomia (CFM) is the most common facial anomaly following cleft lip and palate(1-3). The disorder is characterized by malformations of structures with an embryological origin in the first and second pharyngeal arches and the phenotypic presentation is variable.

The OMENS classification recognizes the most commonly affected facial structures in CFM including the Orbit, Mandible, Ear, Nerve, and Soft-tissues(4). This classification grades the orbital deformity by subjective evaluation of size and position(5). There is inconsistency in the reported incidence and severity of the orbital deformity as well as variability in the correlation between orbital involvement and the type of mandibular deformity(5, 6). These differences may be due to the fact that previous studies used subjective clinical scores of orbital involvement rather than objective measurements of orbital size.

There is lack of correlation between the clinical appearance of the size of the orbit and the volume measured on CT scan (7). To the best of our knowledge there are no papers in the literature that quantitatively measure orbital size in patients with CFM. The purpose of this study was to determine whether there is a difference in orbital volume between affected and unaffected sides in patients with unilateral CFM. The authors hypothesize that the orbit on the affected side will be smaller than that on the unaffected side. The specific aims were to 1) measure orbital volume in patients with CFM 2) compare the volumes of the affected and unaffected sides 3) evaluate the correlation between the clinical evaluation of orbital size and the volumetric measurement and 4) determine whether there is a correlation between orbital volume and severity of mandibular deformity.

Materials and Methods

Study Design

This is a retrospective study of patients with unilateral CFM who had CT images obtained as part of standard clinical care. This study was approved by the Institutional Review Board of the Committee on Clinical Investigation at Boston Children's Hospital (Protocol #X05-08-058) and all research activities were conducted in accordance with the Declaration of Helsinki.

Sample

The study population was composed of all patients presenting for evaluation and management of CFM at Boston Children's Hospital between 1950 and 2015. To be included in the study, subjects had to have unilateral CFM and a CT-scan including both orbits. Patients were excluded if they had undergone a procedure in or around the orbit prior to the first available CT scan or if they had bilateral facial microsomia. The CT scan had to be of serviceable quality in DICOM format and of adequate size, with a slice thickness of 1 mm or less. Therefore, most of the CT scans taken prior to1980 were excluded. All subjects OMENS scores were recorded from the medical record(4).

Data Collection Methods

The DICOM data from CT scans were loaded into 3D segmentation software (Mimics 10.01, Leuven, Belgium). A threshold of -240 to 226 Hounsfield units was used to create a mask that encompassed the soft tissues contained within the orbital cavity but excluded the bony boundaries. The limits of the bony orbit were defined as described by Nout et al (8). The anterior boundary of the orbit was defined in the sagittal plane as a line connecting the most antero-superior points of the supraorabital and infraorbital rims (Image 1). The posterior boundary was defined as the anterior portion of the optic canal. In areas of thin or absent bony walls, a perpendicular line was drawn between the nearest bony boundaries to facilitate segmentation. Manual segmentation was then performed in the sagittal plane on each slice. All measurements were performed in the sagittal plane by one examiner. Orbital volume was automatically calculated from the 3D models of the manually segmented orbit (image 2) (MNG).

Variables

The primary outcome variable was orbital volume. The primary predictor variable was laterality (affected vs. unaffected side). Other variables included orbital and mandibular OMENS scores. Pruzansky-Kaban (9) mandibular types I-IIa were included in group 1 (mild/moderate) and types IIb-III were considered group 2 (moderate/severe), as this is a clinically relevant grouping that determines treatment(10).

Data analysis

Statistical analyses were performed using SPSS/SAS (IBM, 2002) A Wilcoxon signed rank test was used to compare affected and unaffected side measurements within subjects. A subgroup analysis was done to determine if there is a difference in significance of the outcome variable if grouped by severity of mandibular involvement (group 1 and 2). For determination of the correlation between orbital volume and severity of the mandibular deformity a Spearman's rank correlation coefficient was calculated.

Intra-rater and inter-rater agreement were assessed with Intraclass Correlation Coefficients (ICC). ICC>0.8 was considered acceptable reliability. Statistical significance was set at $p \leq 0.05$. Twenty percent of the images were randomly selected for re-measurement by the same examiner at least 2 months after the first evaluation, and for an additional set of measurements performed by a second examiner (BIP).

Results

Patients

Of 238 unilateral CFM patients evaluated during the study period, 39 (23 males and 16 females; mean age 11.5; range 1-44 years) were included (Table 1). The remaining 199 patients were excluded because they either had bilateral facial microsomia, insufficient imaging data or extensive surgical treatment of the orbit or associated bony structures. There were 16 subjects in group 1 (mild/moderate) and 23 in group 2 (moderate/severe).

Orbital Volume

For the entire sample, orbital volume on the affected side was 10 ± 41% smaller than on the unaffected side (mean affected 21501.47 ± 4840.65 mm^3, mean unaffected 22467.42 ± 4179.66 mm^3, p=0.001)(table 1). These differences were statistically significant in both sub-groups (group 1, p=0.021; group 2, p=0.0258) The affected side was smaller than the unaffected side in 80% of the sample.

In subjects with clinically normal sized orbits (OMENS grade O_0 and O_2) CT volumetric measurements found that the affected side was 2 ± 6% smaller than the unaffected side (mean affected 22062.78± 4086.14 mm^3, mean unaffected 22463.77 ± 4333.24 mm^3, p=0.010). The affected side was smaller than the unaffected side in 82%.

There was a negative correlation between orbital volume and severity of the mandibular deformity (orbital volume decreased as the Pruzansky-Kaban severity increased), but this correlation was not statistically significant (p= 0.353).

Intra- and Inter-Rater Agreement

Intra- (0.992) and inter-rater (0.982) reliability were good (ICC>0.8) for all measurements.

Discussion

The purpose of this study was to determine if there is a difference in orbital volume between affected and unaffected sides in patients with unilateral CFM. The specific aims were to 1) measure orbital volume in patients with unilateral CFM 2) compare the affected and unaffected sides 3) evaluate the correlation between the clinical evaluation of orbital size and the volumetric measurement and 4) determine whether there is a correlation between orbital volume and severity of mandibular deformity.

We found that orbital volume on the affected side in most subjects in our sample (80%) was significantly smaller on the affected side. In previous studies where clinical evaluation was used only 4-12% of patients were noted to have small orbits(4, 6, 11). The finding that the orbit is smaller on the affected side is not surprising given that the orbital floor and a portion of the lateral wall are formed by the 1st pharyngeal arch and therefore likely to be hypoplastic. This may result in a decrease in volume and may also explain the orbital dystopia with inferior displacement reported in the majority of patients in the Vento study(4). Tuin(6) and Poon (11)did not differentiate superior from inferior displacement in their analysis.

The average difference between affected and unaffected orbits was small (10%). In our sample 82% of patients who were clinically assessed to have normal orbital size demonstrated volumetric differences on CT; the other 20% had orbits that were similar in volume. Even though differences in orbital size are prevalent in patients with unilateral CFM the small difference may explain the low rate of clinical detection. There were few subjects in our sample who had clinically severe orbital involvement, which may be in part due to exclusion of patients with bilateral craniofacial microsomia and thus the more severe cases.

Previous investigations have tried to correlate the orbital and mandibular deformities. Vento and colleagues (4)showed that abnormalities in orbital position/size were associated with the severity of the mandibular hypoplasia. Tuin (6)reported that the degree of orbital involvement was significantly correlated with the degree of mandibular deformity while Poon (11) documented no association between the deformities. A 2013 study from Wink et al. on maxillary involvement in children with CFM, also showed no association between the severity of the mandibular deformity and maxillary bone volume ratio (12). This inconsistency may be attributed to different study populations. Tuin (6)had the largest population of patients with moderate/severe mandibular deformity and orbital involvement followed by Vento and then Poon(11). Our study population was small and by separating the patients based on the severity of the mandibular deformity we had small samples, which might suggest our sample size per sub-group was insufficient to obtain significant results.

Although grading of the mandibular deformity has progressed over time from a subjective assessment determined by clinical examination, to objective measurement first with postero-anterior cephalograms (9) and more recently with CT scans(13) the assessment of the orbital deformity has been based on clinical examination of size and position. This is the first study to objectively measure orbital volume in patients with CFM. Measuring the position of the orbital cavity using the method previously described in the literature by Nout et al was impossible due to the severe asymmetry of the skull base in patients with unilateral CFM(8, 14).

This study has several limitations including its retrospective nature, small sample size and relatively wide age range of study subjects. We had to exclude

199 patients because of insufficient CT images. Furthermore, using the contralateral side of the patient as a control to the affected side as opposed to a separate control group is also subject to discussion as it is based on the assumption that there is an unaffected side in children with CFM. This has been challenged in the literature as the development of the less affected side in CFM is often not completely normal. It is therefore important that future research is conducted with a normal control group. Although manual segmentation is the gold standard in 3D imaging analysis for orbital volume(15-18) it is labor-intensive and several problems have been encountered when attempting to measure orbital volume using CT-scans. The orbital cavity is a complex conical anatomical structure with thin walls and boundaries that are difficult to define (19). Due to our strict definitions of the bony orbit and the use of previously validated methodology (8), there was good intra- and inter-observer agreement. However, given the nature of the images, it was impossible to blind the examiners to the primary predictor variable (affected versus unaffected side) and it is possible that this introduced some bias. Finally our study would be improved by documentation of globe and/or periorbital tissue measurements as well as the delineating the separate orbital bones and their individual contribution to the smaller orbital volume in patients with CFM.

Conclusion

We found that there was a significantly smaller volume of the affected side in patients with unilateral CFM compared to the unaffected side. Although these differences were small and may not be clinically relevant, they add to a broader understanding of the subclinical spectrum of craniofacial microsomia.

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Image 1. Sagittal CT image demonstrating anterior boundary of orbit

Image 2. 3D models of the orbit

Table 1. Sample characteristics and mean orbital volume

Characteristics	**Value**	
Sample, n	39	
Mean age in years	11,5 (range 1-44, median 9)	
Sex, n		
Male	23	
Female	16	
Pruzansky- Kaban classification, n		
Type 1	6	
Type 2a	10	
Type 2b	16	
Type 3	7	
O in OMENS classification, n		
O_0	32	
O_1	5	
O_2	1	
O_3	1	
Mean Orbital Volume Affected (SD)	21501.47 (4840.65)	$p = 0.001$
Mean Orbital Volume Unaffected (SD)	22467.42 (4179.66)	
Mean Ratio Affected/Unaffected (SD)	0.9532 (0,133)	